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EXAMINER	
SCHMICKEL, D	
ART UNIT	**PAPER NUMBER**
1814	

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DATE MAILED: 11/10/92

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire three month(s), ____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☐ Claims 1-7 + 27 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-7 + 27 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 9-89)

Claims 1-7 and 27 are under consideration. Claims 8-26 have been canceled by Applicant.

Claims 6, 7 and 27 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim as each is multiplydependent on another multiply dependent claim. For instance claim 6 is dependent on anyone of the claims 1 to 4, and claim 3 is dependent on claim 1 or 2. See MPEP 608.01(n). Accordingly, Claims 6, 7 and 27 not been further treated on the merits.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to the gene encoding urate oxidase. See MPEP 706.03(n) and 706.03(z).

Applicants claim a urate oxidase of particularly high activity or molecules with a substantial homology to it. Applicants have only disclosed a single urate oxidase. It is unclear which of the many enzymes with substantial homology can be purified to such a high purity and have the activity claimed. Without such knowledge as which amino acids are essential for activity and which are not, Applicants have not enabled one of ordinary skill in the art to know which substantially homologous proteins are included in the claims or how make such enzymes.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-5 are rejected under 35 U.S.C. § 103 as being

unpatentable over Laboureur et al. in view of Reedy et al. and Riggs or Neilsen et al. in further view of Janson, or Mannson-Rahemtulla et al., Nakagawa et al., or Berton et al.

Laboureur et al. teach the isolation of the Aspergillus flavus urate oxidase and the medical uses of the protein. They do not teach the expression of the urate oxidase gene from A. flavus.

Reedy et al. teach the isolation of the urate oxidase gene from a rat. In this teaching Reedy et al. also provide a general protocol for isolating the gene that encodes any urate oxidase protein.

Riggs teaches the expression of any heterologous protein that is encoded by an isolated gene by use of that isolated gene in E. coli.

Neilsen et al. teach the expression of a heterologous protein that is encoded by an isolated gene by use of that isolated gene in COS-7 cells.

Janson teaches a general method of affinity purification.

Mannson-Rahemtulla et al., Nakagawa et al., and Berton et al. each teach a method of purification of an eukaryotic oxidase by immunoaffinity purification.

It would have been obvious to a person of ordinary skill in the art at the time of the invention to make A. flavus urate oxidase in large quantities and high purity by expressing the A. flavus urate oxidase gene as taught by Neilsen et al. or Riggs that had been isolated as taught by Reedy et al. from A. flavus as it is well known in the art that recombinant protein expression can result in highly pure proteins in high yield. It would have been further obvious to purify the enzyme by means such as conventional, immunoaffinity or

affinity chromotography.

The combination of the above references is motivated as it has also been shown that A. flavus urate oxidase performs a useful enzymatic reaction. Large amounts of urate oxidase, therefore, would have been known to be useful as enzymes to perform medically useful enzymatic reactions to one of ordinary skill in the art. It would have been obvious to one of ordinary skill in the art to further purify the urate oxidase by conventional, immunoaffinity or affinity methods to obtain a protein of the instant invention as these methods had been successfully used to purify other oxiadases in the past, and use this purified protein as a drug.

This purification would have been motivated by the desire to produce an enzyme with potentially fewer harmful contaminants, and the knowledge that urate oxidase has medical uses as is well known to one of ordinary skill in the art.

Applicants declaration states that affinity chromatography was attempted at a certain pH and buffer concentrations and did not result in the instantly claimed activities. One of ordinary skill in the art would have known to vary the pH, salt concentrations, and buffers in routine experimental design to attempt to purify the enzyme.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dave Schmickel whose telephone number is (703) 308-4206.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

David B. Schmickel Ph.D.

ROBERT A. WAX
SUPERVISORY PATENT EXAMINER
GROUP 180